

# Chikungunya virus: An emerging public health challenge for Pakistan

**Faiz Ahmed Raza**

Senior Research Officer / Centre Incharge, Health Research Institute, National Institute of Health, Tuberculosis Research Centre, King Edward Medical University, Lahore – 54000, Pakistan.

**Correspondence email:** faiz.ahmed.raza@nih.org.pk

Chikungunya is a viral illness caused by the Chikungunya virus (CHIKV), an enveloped single-stranded linear RNA alphavirus belonging to the family *Togaviridae*. The CHIKV is transmitted by the same *Aedes* mosquito (*Ae. aegypti* and *Ae. albopictus*) responsible for transmitting the dengue and Zika viruses to humans.<sup>1</sup> These viruses can co-circulate in an area and concurrent infections are possible in the same person.<sup>1</sup>

CHIKV infections are mostly symptomatic (~80%), and the symptoms are similar to dengue virus infection, with fever and polyarthralgia being the commonest. The Chikungunya fever can be divided into three stages: acute (1-21 days), post-acute (22 to 90 days), and chronic stages (>90 days).<sup>2</sup> However, post-acute and chronic stages are not observed in all patients.<sup>3</sup> The acute stage starts after a very brief incubation period (average 3 days, range 1-12 days) with typical symptoms including high-grade fever (>38.5°C), arthralgia, arthritis with edema and pain, myalgia, headache, a maculopapular rash with cutaneous pruritus (soles and palms), facial edema, and lymphadenopathy. The infection is associated with mild thrombocytopenia, increased levels of liver enzymes, increased C-reactive protein (~50–60 mg/L), and lymphopenia (<1000 cells/mm<sup>3</sup>) being the main findings. Anorexia and asthenia are commonly observed after the subsiding of fever.<sup>3, 4</sup> However, the disease may present atypically (like severe pain even after intake of pain relievers, thrombosis, bleeding, dehydration, decompensation of chronic disease, organ failure) in 0.5% of vulnerable patients (elderly, young children, patients with chronic diseases, pregnant females, etc.).<sup>3</sup>

Rare complications of Chikungunya fever may include myocarditis, retinitis, uveitis, hemorrhages, Guillain-Barré syndrome, nephritis, hepatitis, bullous skin lesions, meningoencephalitis and cranial nerve palsies.<sup>5</sup> One-time infections with CHIKV usually provide lifelong immunity against re-infection.<sup>3-5</sup>

Differential diagnosis of Chikungunya fever from dengue fever is challenging due to similar clinical features. But usually CHIKV infection result in high

fever, severe joint pain, rash, arthritis, and lymphopenia in contrast to dengue infection which results in neutropenia, thrombocytopenia, hemorrhage, shock and death.<sup>5</sup> Laboratory confirmation of the CHIKV infection is carried out through viral cultures or viral nucleic acid detection in human serum/plasma by reverse-transcriptase polymerase chain reaction (RT-PCR) from day 1 to 5 of onset of symptoms. Serum IgM antibodies can be detected after five days of fever (and even earlier) and remain detectable for many months post-infection. A four-fold rise in the titer of CHIKV IgG antibodies in paired sera can be carried out to diagnose current infection.<sup>3</sup>

There is no definite treatment available at the moment to treat Chikungunya fever. Symptomatic treatment is provided to patients to prevent fever, relieve pain, avoid dehydration and organs damage. Among analgesics, acetaminophen is recommended; however, nonsteroidal anti-inflammatory drugs and salicylates are not recommended within two weeks of the disease onset due to the risk of bleeding and Reye's syndrome.<sup>3</sup> Currently, no vaccine is approved to prevent CHIKV infections, but many potential vaccine preparations are being evaluated. More promising results have been shown by live attenuated, single-dose vaccine prepared by Valneva/Karolinska Institute in Phase-III clinical trials. The vaccine was effective in 98.5% of participants, and only mild or moderate adverse events were recorded.<sup>6</sup> It could be assumed that a safe and effective vaccine will soon be available against CHIKV infections.

A seroepidemiological study conducted in Pakistan in the 1980s detected CHIKV antibodies in humans and rodents.<sup>7</sup> Although in this study, CHIKV antibodies were detected in only one participant, the first report indicated co-circulation of CHIKV and other arboviruses locally. However, no outbreaks were recorded during the last three decades until 2016, when cases of a "mysterious" disease started to emerge in Karachi, which was later identified as CHIKV infections.<sup>8</sup> The disease rapidly spread to other provinces and was also detected in the federal capital Islamabad by mid-2017.<sup>9</sup> Another seroepidemiological study detected the co-circulation of CHIKV and DENV in Lahore,

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Rawalpindi, and Peshawar.<sup>10</sup> More recently, in November 2021, several local newspapers reported prevalence of another "mysterious disease" affecting a large number of people along with the ongoing dengue epidemic in Lahore and Karachi.<sup>11-13</sup> The mystery disease had dengue-like symptoms but tested negative for it. Many medical practitioners suspected it as Chikungunya fever; however, the exact diagnosis was not made due to lack of expertise, unavailability of diagnostic facilities, and lack of interest and cooperation by the medical fraternity with the researchers interested in deciphering the mystery.

The co-circulation of multiple arboviruses in Pakistan is a worrisome situation as it will inflict a burden on the already fragile health system. There is an urgent need to develop diagnostic facilities and strengthen vector control and surveillance activities to prevent any future epidemics. To control CHIKV infection, developing an efficacious and affordable vaccine and treatment guidelines are need of time.

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